REMARKS

Claims 10-21, 23-30, 37-42, 45 and 47-58 are pending in the present application. Claims 10 and 23 are in independent form. Claims 10, 12, 13, 14, 15, 17, 18, 20, 21, 23, 28, 37, 38, 39, 40 and 42 are amended. Claims 47-58 are newly-added. Although Applicants believe that claims 1-9 are patentable, claims 1-9 and 32-36 have been cancelled without prejudice in the interest of expediting prosecution of the other claims. In view of the above amendments and following remarks, favorable reconsideration and allowance of the present application is respectfully requested.

Initially, Applicants appreciate the Examiner's acknowledgment that all certified copies pertaining to foreign priority claimed under 35 U.S.C. §119 have been received.

I. OFFICE ACTION FORMALITIES

(a) Applicants note that the Examiner has not indicated whether the drawings filed on June 3, 2004 are accepted or objected to by the Examiner. As there is no discussion in the *Detailed Action* indicating that the drawings are objected to, Applicants will assume that the drawings are acceptable unless indicated otherwise in the next Patent Office communication.

(b) Furthermore, Applicants note that the PTO Form 892 included with the Action lists Yamamoto et al., U.S. Patent No. 6,156,506 instead of Jain et al., U.S. Patent No. 6,165,506, as cited in the Action. Applicants respectfully request that the Examiner provide a PTO 892 Form listing Jain et al., U.S. Patent No. 6,165,506 in the next Patent Office communication.

II. NEWLY-ADDED CLAIMS 47-58

By the present Amendment, Applicants submit that claims 47-58 are newly-added. Applicants submit that support for claims 47-58 may be found, at least, on pages 33-38 of the Specification. Accordingly, Applicants submit that the claims do not introduce new matter.

III. SPECIFICATION OBJECTION

The abstract of the disclosure stands objected to for exceeding the 150 word limit.

By the present Amendment, Applicants submit that the Abstract has been amended to comply with 150 word limit established under Rule 1.72.

Thus, Applicants respectfully request that the Examiner reconsider and withdraw the objection to the abstract.

IV. CLAIM OBJECTION

Claim 16 stands objected to under 37 C.F.R. §1.75(c) as being of improper dependent form for failing to further limit the subject matter of the previous claim.

The rejection states that "[t]he claim recites the use of an aqueous binder in a dry (e.g. void of liquid) granulation process." Action, page 3. Thus, Applicants assume that the Examiner believes the use of an aqueous binder (as recited in claim 16) is improper in a fluid bed dry granulation method (as recited in claim 15). (If Applicants have misunderstood the

grounds for the objection, Applicants request that the Examiner provide further explanation in the next Patent Office communication.)

However, Applicants submit that the use of a fluid bed dry granulation process is not limited to the use of a dry binder. That is, in a fluid bed dry granulation process, the binder may be a liquid, or an aqueous solution.

For example, referring to Fig. 18, Applicants submit that example embodiments teach that,

> ...when the binder 64 is used as the liquid material, it is possible to form the nano particle clumps 61 by clumping the nano particles 60, and it is possible to produce the composite particle 62 according to the present invention by clumping the nano particle clumps 61.
>
> Specifically, first, the liquid material (arrow "S" in Fig. 18), supplied from the liquid material supplying section, into the fluid bed space 13 as shown in a left drawing of Fig. 18. A drop of the sprayed liquid material is so minute that a spray mist diameter of the sprayed liquid material is approximately 10 μm. Thus, the liquid material is solidified in a moment while rising in the fluid bed space 13, and the solidified material becomes fine particles 65. Then, the fine particles 65 are collected in the bag filters 15a and 15b that are positioned on the upper side of the fluid bed space 13.
>
> Here, the fine particles 65 have the following characteristics: in case where the seed particles are the nano particles 60, the binder 64 (that is, the primary carrier 59) adhere to the nano particle 60. Further, in case where the seed particles are the nano particle clumps 61, the binder 64 adheres to the nano particle clump 61.
>
> Specification, page 85, line 12 to page 86, line 8.

Furthermore "...in accordance with the fluid bed dry granulation method, the nano particle clump 61 in a fluid state is dried while spraying liquid binder 64, so that the nano particle clump 61 is secondarily clumped

via the binder 64. Therefore, it is possible to produce the binder-clumping-type composite particle 62a with high efficiency and high quality. Further, likewise, it is also possible to produce the nano particle clump 61 by using the nano particles 60, obtained in accordance with the spherical crystallization, as the seed particles." Specification, page 88, lines 6-15.

In the fluid bed dry granulation method according to the above example embodiments, liquid seed particles (*e.g.*, nano particle clumps 61 or nano particles 60) are dried while being sprayed with a liquid material (*e.g.*, binder 64) to produce fine particles 65 (*e.g.*, composite particle 62 (if the liquid particles are nano particle clumps 61) or nano particle clumps 61 (if the liquid particles are nano particles 60)).

As such, Applicants submit that claim 16 properly limits the features of claim 15. Thus, claim 16 is in proper dependent form.

As such, Applicants respectfully request that the Examiner reconsider and withdraw the objection to claim 16.

V. 35 U.S.C. §112, SECOND PARAGRAPH REJECTIONS

Claims 12, 17, 20, 21, 23, 28, 35, 37, 38, 40 and 42 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which is regarded as the invention. Applicants respectfully traverse the rejections.

With regard to the use of the terminology "in accordance with" in claims 12, 13, 17, 20, 21, 23, 28, 37, 38, 40 and 42, Applicants submits submit that claims have been amended to clarify the claimed subject matter.

More specifically, in claims 17, 20, 23, 40 and 42, the terminology "in accordance with" has been replaced with the term "using." Claims 12, 28 and 37 have been amended to recite "by spherical crystallization." In claims 13, 21 and 38, the terminology "in accordance with" has been deleted.

With regard to the combination step and adhering of claims 17 and 40, Applicants submit that claims 17 and 40 have been amended to clarify the claimed subject matter. Namely, claims 17 and 40 have been amended to recite "adhering the primary particles to a surface of a carrier particle using a dry mechanical particle combining method, wherein said carrier particle is larger than the primary particles in terms of an external diameter."

With regard to the weight percent of the drug powder in claims 7 and 35, Applicants submit that claims 7 and 35 have been cancelled.

Furthermore, claim 28 has been amended to depend from claim 24, which provides proper antecedent basis for the lubricant powder. However, with regard to claim 29, Applicants submit that claim 28 (from which claim 29 depends) provides a proper antecedent basis for the polymer nano particle.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejections to claims 9, 12, 17, 20, 21, 23, 28, 37, 38, 40 and 42.

VI. CITED ART GROUNDS OF REJECTION

A. Claim 1 stands rejected under 35 U.S.C. §102(a) as being anticipated by Ohkuma et al. (hereinafter "Ohkuma"), U.S. Patent No. 7,022,311.; and claims 1-3, 5, 8, 33 and 36 stand rejected under 35 U.S.C. §102(b) as anticipated by Ishizaka et al. (hereinafter "Ishizaka"), U.S. Patent No. 5,336,271.

By the present Amendment, claims 1-3, 5, 8, 33 and 36 have been cancelled. Thus, the rejection of claim 1 over Ohkuma is therefore moot.

B. Claims 4, 6, 9, 32 and 34 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Ishizaka. Applicants respectfully traverse the rejection.

By the present Amendment, claims 4, 6, 9, 32, and 34 have been cancelled without prejudice by this Amendment. The rejection of those claims over Ishizaka is therefore moot.

C. Claims 10-15 and 37-39 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Trofast et al. (hereinafter "Trofast"), WO 95/09616, in view of Jain et al. (hereinafter "Jain"), U.S. Patent No. 6,165,506. Applicants respectfully traverse the rejection.

i. Independent Claim 10.

Amended independent claim 10 relates to a method for producing a drug containing composite particle including a two-step method including a primary particle formation step using nano particles and a combining step in which the primary particles are reversibly collected. Applicants submit

that the art cited in the rejection fails to teach, or suggest, the features recited in amended independent claim 10.

a. Trofast.

The Office Action states that "Trofast et al. teach a method of agglomerating fine drug particles via a dry process such that the agglomerated particles (composite particles) would be able to break up into their substituent particles during inhalation (page 2 lines 10-21, page 4 lines 7-8, page 5 lines 6-9; instant claim 10." Office Action, page 7. However, Applicants respectfully disagree because Trofast fails to teach or suggest a two-step process in which nanoparticles are combined to form primary particles and the primary particles are formed into larger reversible collections.

Trofast is directed to a method for the manufacture of agglomerates, and states:

> Most finely divided powders, such as micronized powders, are light, dusty and fluffy and they can create problems during handling, processing and storing. For particles having a diameter less than 10μm the van der Wahls forces are generally greater than the force of gravity and consequently the material is cohesive. The particles tend to adhere to each other forming non-defined agglomerates. Such powders have very poor free-flowing properties which often make handling and precise metering problematic.
>
> One possible method of making these powders free-flowing or at least improve their flowing properties is to force, in a controlled manner, the primary particles to form larger particles, agglomerates.
>
> * * *

> According to the invention there is provided a method for the manufacture of agglomerates, which comprises subjecting the finely divided particles of the medicament, which could be in admixture with any other ingredient desired to be incorporated into the agglomerates, to mechanical unit operations under certain conditions. More specifically there is provided a method of treatment of a finely divided powdered medicament having a particle size smaller than 10 μm and poor flowing properties to form, in a controlled manner, agglomerates or pellets which are free flowing and which are capable of breaking down to provide the finely divided medicament, comprising the steps of:
>
> a) agglomeration of the powdered medicament having a particle size being smaller than 10 μm by feeding the material to a sieve, causing the finely divided powdered medicament to pass through the apertures of the sieve thereby obtaining agglomerates . . . .
>
> Trofast, page 1, lines 15-25 and page 4, line 26 to page 5, line 9.

Thus, Trofast teaches a <u>one-step method</u> in which agglomerates are formed by passing particles of a finely divided powered medicament through a sieve. The method of claim 10, in contrast, comprises <u>two steps</u>: (i) a primary particle formation step of forming primary particles each of which includes nano particles, and (ii) a step of combining the primary particles with each other so that the primary particles are reversibly collected.

Applicants respectfully submit that nothing in Trofast teaches or suggests that an intermediate-size primary particle be formed from nanoparticles and that such intermediate-size primary particles be combined to form larger-size reversible collections. Indeed, Trofast's method merely involves fine particles being agglomerated to form larger particles, with no intermediate size primary particles being formed.

In addition, the Office Action acknowledges that nothing in Trofast teaches or suggests that the fine drug particles therein are nanoparticles (Office Action, page 7). Thus, Trofast's formation of agglomerates does not teach or suggest "a primary particle formation step of forming primary particles each of which includes nano particles whose average particle diameter is less than 1000 nm" as recited in claim 10.

b. Jain.

Although the Office Action acknowledges that nothing in Trofast teaches or suggests that the fine drug particles therein are nanoparticles (Office Action, page 7), the Office Action cites Jain for the "teach[ing] that drug particles sized less than 1000nm were known in the art at the time of the invention for use in solid dosage forms due to their improved dissolution profile." *Id.*

Applicants respectfully submit that Jain does not cure the deficiency of Trofast with respect to a two-step process in which nanoparticles are combined to form primary particles and then the primary particles are formed into larger reversible collections. For example, assuming for discussion purposes that Trofast's fine drug particles were nanoparticles (e.g., drug particles sized less than 1000nm), and the agglomerations thereof could be considered the intermediate size "primary particles" as recited in claim 10, nothing in Trofast or Jain teaches or suggests that such agglomerations should be combined into reversible collections as recited in claim 10. Thus, at very least, a combination of Trofast with Jain teaches no

more than a one-step method and would fail to yield the "step of combining the primary particles with each other so that the primary particles are reversibly collected" recited in claim 10.

Thus, claim 10 is not rendered obvious by a combination of Jain with Trofast. Because claims 11-15 and 37-39 depend directly or indirectly from claim 10, these claims are also not rendered obvious by a combination of Jain with Trofast.

For the foregoing reasons, withdrawal of the rejection of claims 10-15 and 37-39 over Trofast in view of Jain is respectfully requested.

D. Claims 10, 17-19 and 40-41 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Ishizaka in view of Trofast and Jain; and claims 10, 17-18, 20-21 and 42 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Ishizaka in view of Trofast and Jain and further in view of Bruno et al. (hereinafter "Bruno"), U.S. Patent No. 5,518,187. Applicants respectfully traverse the rejection.

Based on the discussion in the Office Action, the rejections of independent Claim 10 over Ishizaka in view of Trofast and Jain, and further in view of Bruno, are not clear. It appears that the rejections may have been intended to relate more specifically to claims 17-21 and 40-42, each of which depends directly or indirectly from claim 10 and relates to adhering primary particles to a surface of a carrier particle. However, to the extent that the rejection was intended as to claim 10, Applicants submit that no combination of these references renders claim 10 obvious for the reasons discussed below.

As to claims 10, 17-19 and 40-41, the Office Action states that "it would have been obvious to one of ordinary skill in the art at the time of the invention was made to use the agglomeration particles composed of drug nanoparticles taught by Trofast et al. modified by Jain et al. (for their improved dissolution profile as taught by Jain et al. column 2 lines 51-59), as the drug/child particles in Ishikawa." Office Action, page 9.

As to Claims 10, 17-18, 20-21, and 42, the Office Action states that "it would have been obvious to one of ordinary skill in the art to use the milling method of Bruno et al. to improve the dissolution properties in the composite particle made by the method of Ishizaka et al. modified by Trofast et al. and Jain et al." Office Action at page 10.

i. Ishizaka.

The Office Action states that:

> Ishizaka et al. teach a composite particle made by the combination of a drug powder and a core particle powder by mechanical impact (see column 4 lines 25-29, column 6 lines 3-5 and 12, and column 7 lines 37-42; instant claim 17). Ishizaka et al. go on to teach that the starch, as the parent or core particle, ranges in size from 0.5μm to 1mm and that the child particles (drug) that are fixed to the surface are smaller in size (see column 3 lines 57-58 and column 4 lines 40-47; instant claims 18-19 and 40-41). Thus, when the size of the starch particles is in the lower end of the range (e.g., 0.5μm) the drug particles are less than 500nm in size.
>
> Office Action, page 9.

Applicants respectfully submit that Ishizaka fails to teach or suggest the "combining step of combining the primary particles" into reversible collections recited in claim 10. Ishizaka's method ends after the child particles (*i.e.*,

ibuprofen particles and polyethylene glycol particles) are fixed to the surface of the starch carrier particle. *See, e.g.*, Ishizaka, column 6, lines 3-40. Assuming for discussion purposes that the end product (*i.e.*, drug- and PEG-coated starch particles) of the Ishizaka method could be considered a "primary particle" as recited in claim 10, nothing in Ishizaka teaches or suggest that such drug- and PEG-coated starch particles should then be "combined with each other so that the primary particles are reversibly collected."

Further, nothing in Ishizaka teaches or suggests that the individual child particles should be formed into reversible collections. Indeed, Ishizaka teaches away from creation of reversible collections of child particles. Ishizaka states that the purpose of his invention is "to provide an improved method for fixing a crystalline organic compound in an amorphous state on core particles, and further for maintaining the composite state between the crystalline organic compound and the core particles by inhibiting the recrystallization of the crystalline material." Ishizaka, column 2, lines 9-16. According to Ishzaka, this purpose is effected by:

> fixing the crystalline organic compound and a hydrophilic polymer compound on the surface of the core particles by impact application in a high velocity gas stream, so as to increase the proportion of the compound which remain amorphous compared to the conventional dry processes for forming composite particles and suppress the change of the amorphous portion of the otherwise crystalline organic compound into a crystalline state . . . so as to form a solid solution in which the crystalline organic compound is mixed and dispersed into the hydrophilic polymer compound on a molecular level.
>
> Ishizaka, column 2, lines 18-26, 33-36; *see also* column 2, lines 27-40, 41-55, ad 56-68.

Ishizaka explains that ibuprofen that is not fixed in "solid solution" with polyethylene glycol "will recrystallize after some time has elapsed." Ishizaka, column 10, lines 6-27. Thus, Applicants submit that a "reversible" collection of child particles (*i.e.*, ibuprofen and polyethylene glycol) would defeat the purpose of fixing the amorphous drug in polyethylene glycol to prevent re-crystallization.

Thus, Ishizaka fails to teach or suggest the "step of combining the primary particles with each other so that the primary particles are reversibly collected" recited in claim 10. As Ishizaka does not address the placement of the end product of its process (*i.e.*, drug- and PEG-coated starch particles) onto a carrier particle, Ishizaka also fails to teach or suggest "adhering the primary particles to a surface of a carrier particle" as part of the combining and reversible collection step as recited in claim 17.

ii. Trofast.

Trofast, which, as discussed above, fails to teach or suggest a two-step method as recited in claim 10, does not remedy the deficiencies of Ishizaka. For example, Applicants respectfully submit that nothing in Trofast teaches or suggests that the child particles of Ishizaka should be first combined or mixed with each other to form "primary particles," that primary particles composed of Ishizaka's child particles should be combined into reversible collections, or that Ishizaka's child particles should be combined into reversible collections.

In addition, as Trofast does not address the placement of the end product of its process (*i.e.*, the agglomerations) onto a carrier particle, Applicants respectfully submit that nothing in Trofast teaches or suggests

"adhering the primary particles to a surface of a carrier particle" as part of the combining and reversible collection step as recited in claim 17.

iii. Jain.

The Office Action cites Jain for the "improved dissolution profile" of drug particles sized less than 1000nm. Applicants respectfully submit that Jain does not cure the deficiencies of Ishizaka or Trofast discussed above. For example, Applicants respectfully submit that nothing in Jain teaches or suggests that the child particles of Ishizaka should be first combined or mixed with each other to form "primary particles," that primary particles composed of Ishizaka's child particles should be combined into reversible collections, or that Ishizaka's child particles should be combined into reversible collections.

iv. Bruno.

The Examiner cites Bruno for the "teach[ing] that milling is used to modify the surface properties to improve the dissolution properties of particles used in pharmaceuticals" and the use of "other particles that are often used as lubricants (e.g., copolymers of lactide and glycolide) to mill (modify the surface) particles used in pharmaceutical preparations." Applicants respectfully submit that Bruno does not cure the deficiencies of Ishizaka or Trofast discussed above. For example, nothing in Bruno teaches or suggests that the child particles of Ishizaka should be first combined or mixed with each other to form "primary particles," that primary particles composed of Ishizaka's child particles should be combined into reversible collections, or that Ishizaka's child particles should be combined into reversible collections.

As such, Applicants submit that no combination of Ishizaka, Trofast, Jain, and/or Bruno, teach or otherwise suggest (i) a two-step method for producing a composite particle including a primary particle formation step and (ii) a combining step wherein "the primary particles are reversibly collected" as recited in amended independent claim 10, or (ii) the inclusion in the combining step of "adhering the primary particles to a surface of a carrier particle" recited in claim 17. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejections of claims 10, 17-21 and 40-42 over Ishizaka in view of Trofast and Jain and/or further in view of Bruno et al.

D. Claims 23-27, 30 and 45 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Ishizaka in view of Jain and further in view of Ryde et al. (hereinafter "Ryde"), U.S. Patent No. 6,375,986, and Zhu et al. (hereinafter "Zhu"), U.S. Patent Publication No. 2002/0119117. Applicants respectfully traverse the rejection.

i. Independent Claim 23.

Amended independent claim 23 relates to a method for producing a drug containing composite particle including making a mixture, containing "nano particles whose average particle diameter is less than 1000 nm and a drug powder whose average particle diameter is larger than the average particle diameter of the nano particles, into a composite particle." Applicants submit that the cited art fails to teach, or suggest, the features recited in amended independent claim 23.

The Office Action states that "Ishizaka et al. teach a dry method of making a composite particle with a parent or core particle, which ranges in size from 0.5μm to 1mm, and smaller child particles that are fixed to the surface (see column 3 lines 57-58, column 4, line 40-47, and column 6 lines 3-5 and 12-13; instant claim 23)." Office Action, page 10. The Office Action further cites Ryde et al. for "a surface stabilizer (lubricant) is adsorbed to the surface of a drug and both are sized such that the composite is less than about 1μm in size" and Jain et al. for "production of a nanoscale composite pharmaceutical where a surface modifier (lubricant) is adsorbed to the surface of a drug." *Id.*

The Office Action further states that "in order to exploit the improved dissolution properties of nanoscale pharmaceutical components, one of ordinary skill in the art at the time the invention was made would have found it obvious to use the method of Ishikawa to produce a composite particle where a drug served as the parent and a lubricant served as the child, such that the lubricant was less than 1000nm." Office Action, page 11.

Applicants respectfully submit that nothing in Ishizaka, Ryde, or Zhu teach or suggest that drug particles can or should be used as the parent core particles, or that a lubricant can or should be used as a child particle, in the method of Ishzaka.

Ishizaka explains that the "present invention relates to a method for increasing the proportion of the material which is amorphous in a product made of a crystalline organic compound and for suppressing

recrystallization thereof" comprising "formation of a fixed layer of amorphous state from said at least one crystalline organic compound and a hydrophilic polymer substance over the surface of a core particle by means of impact application in a high velocity gas stream." Ishizaka, column 1, lines 10-23.

Ishizaka further explains that the impact application of the crystalline organic compound and hydrophilic polymer compound on the surface of the core particles results in the formation of "a solid solution in which the crystalline organic compound is mixed and dispersed into the hydrophilic polymer compound on a molecular level." Ishizaka, column 2, lines 18-26, 33-36; *see also* column 2, lines 27-40, 41-55, and 56-68. Ibuprofen that is not fixed in "solid solution" with polyethylene glycol "will recrystallize after some time has elapsed." *Id.*, column 10, lines 6-27.

Applicants respectfully submit that nothing in Ishizaka, Ryde, Jain, or Zhu teach or suggest that one should, or successfully could, substitute organic crystalline drug particles for the parent core particles in Ishizaka's method. Indeed, as discussed below Ishizaka teaches away from such a substitution.

As to the material of which the core particle may be made, Ishizaka states:

> As a core particle on which the crystalline organic compound and the hydrophilic polymer substance are supported to form a composite particulate product according to the present invention, the following can be used for example: cellulose products to be used in various medicinal preparations, such as crystalline cellulose, hydroxypropyl cellulose, carboxymethyl cellulose and derivatives of them; starch, such as potato starch, corn starch, wheat starch, partially solubilized starch, dextrin and derivatives of them; sugars, such as milk sugar; and

> synthetic high polymeric materials, such as nylon, polyethylene, polystyrene. Use of inorganic substances may also be possible, for example, a powder of a metal, such as iron, nickel, aluminum, copper; metal oxides, such as alumina, zirconia; and carbides, such as silicon carbide.
>
> Ishizaka, column 3, lines 42-56.

Despite this list of more than 20 exemplary core particle materials, Ishizaka never suggests that the crystal organic drug particles can or should be used as the core particle. This is not surprising considering that Ishizaka's impact application method yields a "solid solution" of drug particles and hydrophilic material in a layer on the surface of a core particle, and that the drugs particles themselves are likely too frangible to serve as a substrate for impact application (*i.e.*, Ishizaka explains that particles of the crystalline compounds "are subjected to a selective crushing in an impact chamber of a particle surface modifying device to be employed for realizing the method according to the present invention." Ishizaka, column 4, lines 6-10. Indeed, without a core particle of the sort described by Ishizaka, upon which to "impact apply" the drug particles and hydrophilic polymer, it is not clear that Ishizaka's "solid solution" of drug particles and hydrophilic material particles can be formed. Thus, there is no reason to modify Ishizaka to substitute drug particles in place of the parent core particles. *See, e.g., In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)(there is no reason for making a modification to prior art if the proposed modification would render such prior art unsatisfactory for its intended purpose).

Moreover, substituting drug particles for the core particle and then attempting to "impact apply" a nanoparticle (such as a lubricant) would not be a practice of Ishizaka's method. As Ishizaka makes clear, the point of the method is to stabilize an amorphous form of the drug and suppress re-crystallization by "formation of a fixed layer of amorphous state from said at least one crystalline organic compound and a hydrophilic polymer substance over the surface of a core particle by means of impact application in a high velocity gas stream." Without a separate core particle upon which to form the "fixed layer . . . over the surface of a core particle," no fixed layer over the surface of a core particle will be formed. Because substituting a drug particle for the core particle in Ishizaka would result in a different process than that described by Ishizaka, and a process that would not necessarily serve the purpose of Ishizaka's method, there is no reason to modify Ishizaka in that way. *See, e.g., In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984); *Ex Parte Charette et al.*, Appeal 2008-0236, Appln. No. 10/064,731 (BPAI June 4, 2008)(invention not obvious where objective of cited prior art sound sensor invention was to "eliminate subjectivity and evaluate sounds based on fixed criteria" and claims-at-issue recited step of subjectively evaluating object to determine source of sound).

Ishizaka further explains that, for the hydrophilic material, "it is preferable to select a substance which easily forms a solid solution with the crystalline organic compound employed and which does not easily form a solid solution with the material of the core particle." Ishizaka at col. 4, lines 11-15. Substituting the drug particle for the core particle is antithetical to

this teaching because the drug particle is intended to form a solid solution with the hydrophilic material. Thus, Ishizaka teaches away from using the drug particles as the core particle. *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740, 167 L.Ed.2d 705 (2007)("when the prior art teaches away from combining certain known elements, discovery of a successful means of combining them is more likely to be nonobvious")(citing *United States v. Adams*, 383 U.S. 39, 40, 86 S.Ct. 708, 15 L.Ed.2d 572 (1966)); *see also In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984), *Ex Parte Charette et al.*, Appeal 2008-0236, Appln. No. 10/064,731 (BPAI June 4, 2008).

For these reasons, Applicants submit that Ishizaka, individually or in combination with Ryde, Jain, and/or Zhu, fail to teach, or suggest, a method for producing a drug containing composite particle including making a mixture containing "nano particles whose average particle diameter is less than 1000 nm and a drug powder whose average particle diameter is larger than the average particle diameter of the nano particles, into a composite particle" as recited in amended independent claim 23.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection to independent claim 23, and claims 24-27, 30 and 45 at least by virtue of their dependency on independent claim 23.

VII. DOUBLE PATENTING REJECTION

Claims 1 and 23-24 stand rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 12 and 16 of U.S. Patent No. 7,022,311 ("the '311 Patent"). Applicants respectfully traverse the rejection.

The Officer Action states that "[a]lthough the conflicting claims are not identical, they are not patentably distinct form each other because both claim a dry process of making a composite particle with a drug and carrier/surface modifier/nano particle where the carrier is taught to be less than 1000nm (see claim 17). It would have been obvious to one of ordinary skill in the art to use the teachings of claim 17 of Patent No. 7,022,311 to practice the method of claims 12 and 16." Action, page 12. Applicants respectfully disagree for the following reasons.

A. INDEPENDENT CLAIM 23

Applicants submit that claim 4 of the '311 Patent (from which claims 12 and 16 depend) recites "said micronized surface modifier has a mean particle diameter of 1.5μm." Thus, claims 12 and 16 are limited to micronized surface modifiers of mean particle diameter of 1.5μm, well above the size of the recited "nano particles whose average particle diameter is less than 1000 nm." In contrast, claim 17 of the '311 patent depends from claim 1, which includes a Markush group the members of which (i) do not include any mean particle diameter limitation, or (ii) a mean particle diameter limitation of not more than 3 μm. Claim 17's recitation of a mean particle

diameter of 0.1 to 3 μm therefore does not relate to claims 12 and 16, and does not (indeed, cannot) teach or suggest that those claims cover embodiments having mean particle diameters of 0.1 μm. Thus, Applicants submit that claims 12 and 16 of the '311 Patent fail to explicitly teach, or otherwise suggest, "nano particles whose average particle diameter is less than 1000 nm" as recited in independent claim 23.

In addition, claims 12 and 16 fail to teach, or suggest, that micronized active ingredient has an average particle diameter larger than the micronized surface modifier. Thus, Applicants submit that claims 12 and 16 of the '311 Patent also fail to explicitly teach, or otherwise suggest "a drug powder whose average particle diameter is larger than the average particle diameter of the nano particles" as recited in independent claim 23.

B. DEPENDENT CLAIM 24

In addition to the above-cited deficiencies of the '311 patent as to independent claim 23, from which claim 24 depends, claims 12 and 16 of the '311 Patent further fail to explicitly teach, or otherwise suggest, that the micronized surface modifier lubricates the micronized active ingredient. Thus, "a lubricant powder is used as the nano particles" as recited in dependent claim 24 is not obvious over claims 12 and 16 of the '311 Patent.

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CONCLUSION

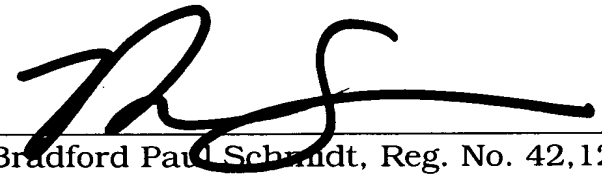
Accordingly, in view of the above, reconsideration of the rejections and allowance of each of claims 10-21, 23-30, 37-42, 45 and 47-58 in connection with the present application is earnestly solicited.

Should there be any matters that need to be resolved in the present application; the Examiner is respectfully requested to contact the undersigned at the telephone number below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 08-0750 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

HARNESS, DICKEY, & PIERCE, P.L.C.

By 
Bradford Paul Schmidt, Reg. No. 42,128

P.O. Box 8910
Reston, Virginia 20195
(703) 668-8000

BPS/CDW:psy